Title	Expression of macrophage migration inhibitory factor in Helicobacter pylori-induced gastritis and peptic ulcer disease
Author(s)	Xia, HHX; Wong, BCY; Huang, XR; He, XX; Wong, WM; Leung, SY; Yuen, ST; Lan, HY; Lam, SK
Citation	The 7th Medical Research Conference, Hong Kong, China, 26-27 January 2002, v. 24 n. 2 Supp, p. 41
Issued Date	2002
URL	http://hdl.handle.net/10722/48477
Rights	Creative Commons: Attribution 3.0 Hong Kong License

C-GH-4

Expression of Macrophage Migration Inhibitory Factor in *Helicobacter pylori*-Induced Gastritis and Peptic Ulcer Disease

HHX Xia,[1] BCY Wong,[1] XR Huang,[2] XX He,[1] WM Wong,[1] SY Leung,[3] ST Yuen,[3] HY Lan[2] & SK Lam[1]
[1]Departments of Medicine and [3]Pathology, The University of Hong Kong, Queen Mary Hospital, Hong Kong, & [2]Department of Medicine, Baylor College of Medicine, Houston, USA

Introduction: Macrophage migration inhibitory factor (MIF) plays a pivotal role in inflammatory/immune diseases. However, its role in *H. pylori*-induced gastritis and peptic ulcer disease has rarely been investigated. This study aimed to determine the association between *H. pylori* infection and expression of MIF.

Methods: 34 patients (M/F, 18/16, age, 53 ± 17 (mean +/-SD) yrs) referred for upper endoscopy were included; 12 with peptic ulcers and 22 with non-ulcer dyspepsia (NUD). Gastric antral biopsies were obtained for the detection of *H. pylori* infection, histological examinations according the update Sydney System, double immunostaining for MIF/T-cells (CD45RO) and MIF/macrophage (KP1), and *in situ* hybridization for the expression of MIF mRNA in the gastric mucosa.

Results: *H. pylori* was detected in 21 (62%) patients; 10 with ulcers and 11 without. There was a significant difference in the numbers of overall T-cells (2076 ± 277/mm2 (mean+/-SE) vs 978 ± 131/mm^2, P=0.001), MIF+ T-cells (1566 ± 252/mm^2 vs 656 ± 105/mm^2, P=0.003), overall macrophages (1220 ± 163/mm^2 vs 223 ± 72/mm^2, P<0.001), MIF+ macrophages (454 ± 74/mm^2 vs 66 ± 25/mm^2, P<0.001) and MIF mRNA+ cells (3518 ± 390/mm^2 vs 200 ± 46/mm^2, P<0.001) between *H. pylori* positive and negative patients. The numbers were also significantly higher in ulcer patients than in NUD patients. Using a univariate general linear model, *H. pylori* infection was identified as an independent risk factor for the increase of all the five parameters while the presence of ulcers was only for the increase of macrophages. Increase in all the five parameters was associated with active and chronic gastritis (all P<0.05). Moreover, in the presence of intestinal metaplasia the numbers of MIF+ T-cells (P=0.18), MIF+ macrophage (P=0.026 and MIF mRNA+ cells (P=0.09) was increased.

Conclusions: *H. pylori* infection causes gastritis and peptic ulcer, partly by stimulating the expression of MIF. Over-expression of MIF may also play a role in the development of intestinal metaplasia, indicating its important role in gastric carcinogenesis.

C-GH-5

Factors Predicting Hepatitis B Virus DNA Breakthrough in Patients Receiving Prolonged Lamivudine Therapy

M.F. Yuen,[1] E. Sablon,[2] C.K. Hui,[1] H.J. Yuan,[1] H. Decraemer,[2] C.L. Lai[1]
[1]Department of Medicine, Faculty of Medicine, The University of Hong Kong; [2]Innogenetics N.V., Ghent, Belgium

Introduction: Lamivudine is widely used as a treatment of chronic HBV infection, because it can profoundly suppress HBV replication and result in significant histological improvement. However long-term lamivudine therapy has been reported to be associated with mutation of YMDD motif in the C domain of HBV DNA polymerase gene. This study was performed to identify the factors predicting the chance and severity of hepatitis B virus (HBV) DNA breakthrough as well as the significance of YMDD variants without the presence of wild-type YMDD on prolonged lamivudine treatment.

Method: 159 chronic HBV patients with lamivudine therapy were recruited from previous clinical studies. HBsAg and HBeAg were tested by ELISA. HBV DNA at every follow-up was detected by the branched DNA assay with a lower limit of detection at 700,000 copies/ml. HBV DNA level at 6 months of lamivudine treatment were measured by a more sensitive assay, Cobas Amplicor HBV Monitor Test with a lower limit of detection at 200 copies/ml. The genotype of the YMDD motif was tested by the line probe assay (INNO-LiPA HBV DR).

Results: Pretreatment baseline HBV DNA levels and ALT levels were inversely correlated with the time of HBV DNA breakthrough with YMDD variants (r=-0.46, p=0.001; r=-0.45, p=0.001 respectively). Patients harboring YMDD variants 3 months before HBV DNA breakthroughs had significantly higher HBV DNA breakthrough levels compared to those without YMDD variants 3 months before HBV DNA breakthroughs (18.9×10^6 vs. 5.4×10^6 copies/ml, p=0.007). 13 of 22 (59.1%) patients who harbored the YMDD variants 3 months before HBV DNA breakthrough had changed the viral population at the time of HBV DNA breakthrough. At six months of lamivudine therapy, only 12 patients (7.5%) had undetectable HBV DNA level using Cobas Amplicor HBV Monitor Test. Patients with HBV DNA levels of more than 10^3 copies/ml at 6 months of lamivudine therapy had a 63.2% chance of developing YMDD variants. HBeAg seroconversion occurred in 26 patients. HBeAg seroconversion occurred in 2 patients after the emergence of YMDD variants, and one patient developed YMDD variant after HBeAg seroconversion.

Conclusion: We conclude that patients with higher baseline ALT level and higher HBV DNA level would have a higher chance and earlier time to develop HBV DNA breakthrough. Patients with YMDD mutation detected 3 months before HBV DNA breakthrough would have higher HBV DNA level at the time of breakthrough.